

Winter 2015 Newsletter



Informaticians on the "Precision Medicine" Team

My first recollection of the term "Precision Medicine" (PM) is from a [talk](#) by Harvard Business School's Clayton Christensen on disruptive technologies in healthcare and personalized medicine in 2008. He contrasted precision medicine with intuitive medicine, saying, "the advent of molecular diagnostics enables precision medicine by allowing physicians to delineate conditions that are likely constellations of diseases presenting with a handful of symptoms." The term became mainstay after [NRC's report](#), "Toward precision medicine: Building a knowledge network for biomedical research and a new taxonomy of disease." Now, we converge on the [NIH's definition](#) – PM is an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle.

"Cures for major diseases including cancer are within our reach if only we have the will to work together and find them. Precision medicine will be the way forward," says Dr. John Marshall, head of GI Oncology at MedStar Georgetown University Hospital.

The main question in my mind is: **How can we apply PM to improve health and lower cost?** Many sectors/organizations are buzzing with activity around PM to help answer this question.

NIH is developing focused efforts in cancer to explain drug resistance, genomic heterogeneity of tumors, monitoring outcomes and recurrence and applying that

Mark Your Calendar

2/26/2015 - ICBI is holding its next **Meet Up** on February 26th on Georgetown University's campus in St. Mary's Hall Room 107 from 6:15 - 8:00pm. Our speakers will be Dr. Luciane Cavalli from Georgetown University and Dr. Vahan Simonyan from the Food and Drug Administration. To see details and register, visit [Biomedical Data Science Meetup](#) and join the group!

10/16/2015 - ICBI's 4th Annual Biomedical Informatics Symposium will be held on Friday, October 16, 2015 at the Georgetown University Conference Center. [Isaac Kohane, MD, PhD](#), Harvard University will deliver the keynote address. Click [here](#) to see highlights from last year's event.

ICBI in the Community

ICBI members participated in the following recent conferences and events:

Posters

G-DOC *Plus*: A cloud based next-generation systems medicine platform for precision medicine (Yuriy Gusev, Krithika Bhuvaneshwar, Anas Belouali, Varun Singh, Robert M Johnson, Lei Song, Shruti Rao, Adil Alaoui, Michael A. Harris, Robert Clarke and Subha Madhavan) **AACR Computational and Systems Biology of Cancer Conference** - San Francisco, February 2015

"A systems biology approach to understanding estrogen responsiveness in breast cancer cells using the MCF7 model" (Ayesha N. Shajahan-Haq, Lang Li, Yunlong Liu, Lu Jin, David F. Miller, Jay Pilrose, Amrita Cheema, Simina Boca, Krithika Bhuvaneshwar, Subha Madhavan, Robert Clarke and Kenneth P. Nephew). **AACR Computational & Systems Biology of Cancer Conference** - San Francisco, Feb 2015

"Early growth response (EGR1) is a critical regulator of cellular metabolism and predicts increased responsiveness to antiestrogens in breast cancer" (Ayesha N. Shajahan-Haq, Lu Jin, Amrita K. Cheema, Simina Boca, Yuriy Gusev, Krithika Bhuvaneshwar, Diane M. Demas, Habtom Resson, Ryan Michalek, Xi Chen, Jianhua Xuan, Subha Madhavan and Robert Clarke) **AACR Computational and Systems Biology**

knowledge in the development of more effective approaches to cancer treatment. In a recent [NEJM article](#), Drs. Collins and Varmus describe NIH's near-term plan for PM in cancer and a longer-term goal to generate knowledge that is broadly applicable to other diseases (e.g., inherited genetic disorders and infectious diseases). These plans include an extensive characterization and integration of health records, behavioral, protein, metabolite, DNA, and RNA data from a longitudinal cohort of 1 million participants. The cost for the longitudinal cohort is roughly \$200M to expand trials of genetically tailored treatments, explore cancer biology, and set up a "cancer knowledge network" for sharing this information with researchers and oncologists.

FDA is working with the scientific community to ensure that the public can be confident that genomic testing technology is safe and effective while preserving innovation among developers. The FDA recently issued [draft guidance](#) for a framework to regulate laboratory-developed tests (LDTs). Until now, most genomic testing is done through internal custom developed assays or commercially available LDTs. The comment period just ended on Feb 2.

Pharma/Biotech companies are working to discover and develop medicines and vaccines to deliver superior outcomes for their customers (patients) by integrating "Big Data" (clinical, molecular, multi-omics including epigenetics, environmental, and behavioral information).

Providers, health systems, and Academic Medical Centers are incorporating appropriate molecular testing in the care continuum and actively participating in clinical guideline development for PM testing and use.

Public and private Payors are working to appropriately determine clinical utility, value and efficacy of testing to determine reimbursement levels for molecular diagnostic tests – a big impediment for PM testing right now. Payors recognize that collecting outcomes data is key to determining clinical utility and developing appropriate coding and payment schedule.

Diagnostic companies are developing and validating new diagnostics to enable PM, especially capitalizing on the new value-based reimbursement policies for drugs. They are also addressing joint DX/RX approval processes with the FDA.

Professional organizations are setting standards and guidelines for proper use of "omics" tests in a clinical setting – examples include AMA's CPT codes, ASCO's QOPI guidelines, or NCCN's compendium.

Many technology **startups** are disrupting current models in targeted drug development and individualized patient care to deliver on the promise of PM. [mHealth](#) domain is

of Cancer Conference -San Francisco, Feb. 2015

Talks

Evidence framework for cancer biomarker curation for precision medicine research – **Dana-Farber Cancer Institute, Harvard University**, Jan. 2015 - Boston, MA

Data Science Platforms for Molecularly Targeted Therapy and Precision Medicine Research – **University of Pittsburgh**, Feb. 2015, Pittsburgh, PA

News and Media

[AMIA 2016 Symposium - Joint Summits and iHealth Chairs Selected](#) - AMIA E-News

[Amarantus Options Blood-based Alzheimer's Biomarkers from Georgetown](#) - Genome Web

[Looking Ahead - Using EHR Data to Better Inform Treatment](#) - AABB News

New Initiatives

NVIDA Grant: The ICBI Data Visualization Lab was made possible through hardware grants from the NVIDIA Corporation and the Georgetown University Information Services Research Technologies group. The system is capable of displaying over 16 million pixels allowing for the visual exploration of vast biomedical data sets.

Primary Care Coalition: ICBI in collaboration with Howard University received a GHUCCTS grant to partner with the Primary Care Coalition of Montgomery County (PCC), a community-based healthcare system that strives for universal access and health equity for the underserved. PCC works with a network of 12 primary care community clinics in Montgomery County that serve low-income, uninsured, and ethnically diverse patients. The project's objective is to assist with cohort discovery, analytical capabilities and methodologies to enhance the health status of most disadvantaged communities. The team will engage investigators from PCC and GHUCCTS to facilitate trials on personalized medicine usage, resource utilization and address barriers to implementing community-based health programs that will ultimately enhance outcomes for the county's vulnerable populations.

CardioTox: ICBI is collaborating with Dr. Paula Pohlmann, MD, PhD and Ana Barac, MD, PhD on a study to identify breast cancer patients within the MedStar Health system at high risk for cardiotoxicity due to HER2 directed therapies and anthracycline administration. Both molecular (biomarker) and clinical data will be used to develop a predictive model to

rapidly expanding with innovative mobile sensors and wearable technologies for personal medical data collection and intervention.

As **informaticians and data scientists**, we have a tremendous opportunity to collaborate with these stakeholders to contribute in unique ways to PM:

1. Develop improved decision support to assist physicians in taking action based on genomic tests.
2. Develop common data standards for molecular testing and interpretation
3. Develop methods and systems to protecting patient privacy and prevent genetic discrimination
4. Develop new technologies for measurement, analysis, and visualization
5. Gather evidence for clinical utility of PM tests to guide decisions on utility
6. Develop reference databases on the molecular status in health and disease
7. Develop new paradigms for clinical trials (N of one trials, basket trials, adaptive designs, other)
8. Develop methods to bin patients by mutations and pathway activation rather than by tissue site alone.
9. Create value from Big Data
10. ...

What are your ideas? What else belongs on this list?

Jessie Tenenbaum, Chair, AMIA Genomics and Translational Bioinformatics shares: "It's an exciting time for informatics, and translational bioinformatics in particular. New methods and approaches are needed to support precision medicine across the translational spectrum, from the discovery of actionable molecular biomarkers, to the efficient and effective storage and exchange of that information, to user-friendly decision support at the point of care."

A PricewaterhouseCoopers [analysis](#) predicts the total market size of PM to hit between \$344B-\$452B in 2015. This includes products and services in molecular diagnostics, nutrition and wellness, decision support systems, targeted therapeutics and many others. For our part, at ICBI, we continue to develop tools and systems to accurately capture, process, analyze, and visualize data at patient, study, and population levels within the Georgetown Database of Cancer ([G-DOC](#)). "Precision medicine has been a focus at Lombardi for years, as evidenced by our development of the G-DOC, which has now evolved into G-DOC Plus. By creating integrated clinical and molecular databases we aim to incorporate all relevant data that will inform the care of patients," commented Dr. Lou Weiner, Director, Lombardi

identify patients at high risk for cardiotoxicity.

Center for New Designs in Learning and Scholarship (CNDLS): This is a grant funded by the Initiative on Technology Enhanced Learning (ITEL) grant. Project Title: In class immersion of "Big Data" technologies to improve students' understanding of Genomic Instability and Systems Biology 1/1/2015 - 3/12/2015; Co-PIs: Ronit Yarden, Jan LaRocque, Yuriy Gusev

Hyundai Hope On Wheels: ICBI is collaborating with Dr. Sadhna Shankar, MD (INOVA) and Dr. John Deeken, MD (INOVA) to integrate whole genome and whole exome sequencing data with clinical and pre-clinical data sets to identify, test, and validate a pharmacogenetic 'resistant' genotype to cisplatin, doxorubicin, and methotrexate (MAP) in pediatric osteosarcoma patients. The goal of the project is to develop a germline pharmacogenetic profile which can be used to predict sensitivity or resistance to therapy and provide personalized cancer therapy.

Recent Publications

Rupak Pathak, Amrita Cheema, Simina Boca, Kimberly Krager, Martin Hauer-Jensen, Nukhet Aykin-Burns. Modulation of Radiation **Response** by the **Tetrahydrobiopterin Pathway**. *Antioxidants* 2015, 4(1), 68-81.

Edwards, Nathan; Oberti, Mauricio; Thangudu, Ratna; Cai, Shuang; McGarvey, Peter; Jacob, Shine; Madhavan, Subha; Ketchum, Karen. **The CPTAC Data Portal: A Resource for Cancer Proteomics Research**. *Journal of Proteome Research* (submitted)

Peter B McGarvey, Baris E Suzek, James N Baraniuk, Shruti Rao, Brian Conkright, Samir Lababidi, Andrea Sutherland, Richard Forshee, and Subha Madhavan. **In silico analysis of autoimmune diseases and genetic relationships to vaccination against infectious disease**. *BMC Immunol.* 2014 Dec 9;15(1):61.

ICBI Consultation and Support

ICBI offers biomedical informatics and clinical

Comprehensive Cancer Center who was invited to the White House precision medicine rollout event on January 30.

Other ICBI efforts go beyond our work with Lombardi. With health policy experts at the [McCourt School of Public Policy](#), we are working to identify barriers to implementation of precision medicine for various stakeholders including providers, LDT developers, and carriers. Through our collaboration with [PRSM](#), the regulatory science program at Georgetown, and the FDA, we are cataloging SNP population frequencies in world populations for various drug targets to determine broad usefulness of new drugs. And through the [ClinGen](#) effort, we are adding standardized, clinically actionable information to variant databases.

The President's recent [announcements](#) on precision medicine have raised awareness and prompted smart minds to think deeply about how PM will improve health and lower cost. We are one step closer to realizing the vision laid out by Christensen's talk in 2008. ICBI is ready for what's next.

Let's continue the conversation – find me on e-mail at subha.madhavan@georgetown.edu or on twitter at [@subhamadhavan](#)

informatics services to the GU community. ICBI staff would love to collaborate with you to provide advice on choosing which analyses could be most insightful for your studies and help run your data through our bioinformatics pipelines to help answer your research questions. Some of the diverse and exciting projects we are collaborating with GU and external investigators are: Systems biology approach to evaluate biomarkers of safety and immune protection for genetically modified live attenuated Leishmania vaccines (Sreenivas Gannavaram, FDA), Systems biology and Network analysis for mTOR signaling pathways in bladder cancer (Donna Hansel, MD, PhD, UC San Diego), NGS data analysis for GI cancer (Ruth He, PhD), and Correlation analysis related to BRCA1 (Ronit Yarden, PhD).

ICBI is working with Lombardi's Biospecimen task force chartered by Dr. Michael Atkins, Deputy Director, Lombardi Comprehensive Cancer Center, to integrate tissue resources from histopathology, non-therapeutic and tissue culture shared resources through a biospecimen dashboard. An initial version of the software was released to beta testers in January. The dashboard is expected to be widely available to Lombardi researchers in Spring, 2015.

As part of our clinical informatics services, we offer patient data extraction from EHRs, REDCap database setup and clinical study data management services. REDCap is a secure web-based application for building and managing online surveys. ICBI currently hosts and provides support to 160 REDCap projects and 379 active users. We facilitate access to over 7 million patient records from MedStar Health hospitals, Howard University hospital, and Veterans Affairs DC Medical Center. Our HIPAA-certified and trained data managers collaborate with researchers and clinicians at GU to access PHI data from EHRs and help them with data analysis. Currently our collaborators are using this service for outcomes, quality of life, and adverse events research.

You can contact us for bioinformatics and research support consultation at:
<http://icbi.georgetown.edu/support>